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=> b reg
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DICTIONARY FILE UPDATES:   8 MAY 2009  HIGHEST RN 1144618-76-7

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http://www.cas.org/support/stngen/stndoc/properties.html

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L4              STR
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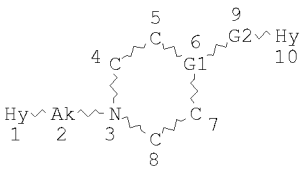


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REP G2=(0-7) C
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DEFAULT ECLEVEL IS LIMITED
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ECOUNT  IS E8 C  E1 O  AT  10

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  10

STEREO ATTRIBUTES: NONE
L6         9239 SEA FILE=REGISTRY ABB=ON  PLU=ON  NC4-C6/ES AND OC4-C6/ES
L8          192 SEA FILE=REGISTRY SUB=L6 SSS FUL L4

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SEARCH TIME: 00.00.01



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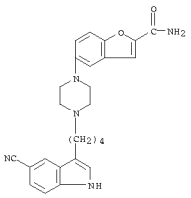
FILE COVERS 1907 - 11 May 2009 VOL 150 ISS 20
FILE LAST UPDATED: 8 May 2009 (20090508/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2009

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

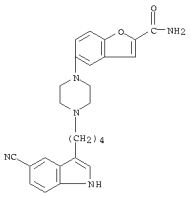
=> d bib abs hitrn fhitstr l48 tot

L48 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:578527 HCAPLUS
DN 143:126601
TI Effect of vilazodone on 5-HT efflux and re-uptake in the guinea-pig dorsal raphe nucleus
AU Roberts, Claire; Hagan, Jim J.; **Bartoszyk, Gerd D.**; Kew, James N. C.
CS Psychiatry CEDD, GlaxoSmithKline, Harlow, Essex, CM19 5AW, UK
SO European Journal of Pharmacology (2005), 517(1-2), 59-63
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier B.V.
DT Journal
LA English
AB The effect of vilazodone, a putative selective serotonin re-uptake inhibitor (SSRI) with 5-HT (5-hydroxytryptamine)1A receptor partial agonist activity, was investigated on 5-HT efflux and 5-HT re-uptake half life in the guinea-pig dorsal raphe nucleus, using in vitro fast cyclic voltammetry. The SSRI, fluoxetine, significantly increased 5-HT efflux. In contrast, vilazodone had no effect on 5-HT efflux at 100 nM but significantly decreased 5-HT efflux at 1 μM. Co-perfusion of 8-OH-DPAT (± 8-hydroxy-2-(di-n-propylamino)tetralin) with fluoxetine significantly attenuated the fluoxetine-induced increase in 5-HT efflux. Co-perfusion of WAY 100635 with vilazodone did not attenuate the effect of vilazodone alone. In addition, the re-uptake half life for 5-HT was significantly increased by both fluoxetine and vilazodone. In conclusion, we have demonstrated that vilazodone (100 nM, 1 μM), in the guinea-pig dorsal raphe nucleus, blocks the serotonin transporter but does not display 5-HT1A receptor agonism.
IT **163521-12-8**, Vilazodone
RL: PAC (Pharmacological activity); BIOL (Biological study)
(effect of vilazodone on 5-HT efflux and re-uptake in the guinea-pig dorsal raphe nucleus)
IT **163521-12-8**, Vilazodone
RL: PAC (Pharmacological activity); BIOL (Biological study)
(effect of vilazodone on 5-HT efflux and re-uptake in the guinea-pig dorsal raphe nucleus)
RN 163521-12-8 HCAPLUS
CN 2-Benzofurancarboxamide, 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]- (CA INDEX NAME)



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)



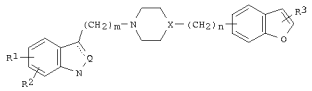
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:184699 HCAPLUS
DN 142:329682
TI Neurochemical evaluation of the novel 5-HT1A receptor partial agonist/serotonin reuptake inhibitor, vilazodone
AU Hughes, Zoe A.; Starr, Kathryn R.; Langmead, Christopher J.; Hill, Matthew; **Bartoszyk, Gerd D.**; Hagan, James J.; Middlemiss, Derek N.; Dawson, Lee A.
CS Psychiatry CEDD, Glaxo Smith Kline, Neuropharmacology Research, Essex, CM19 5AW, UK
SO European Journal of Pharmacology (2005), 510(1-2), 49-57
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier B.V.
DT Journal
LA English
AB Vilazodone has been reported to be an inhibitor of 5-hydroxytryptamine (5-HT) reuptake and a partial agonist at 5-HT1A receptors. Using [35S]GTPγS binding in rat hippocampal tissue, vilazodone was demonstrated to have an intrinsic activity comparable to the 5-HT1A receptor agonist 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT). Vilazodone (1-10 mg/kg p.o.) dose-dependently displaced in vivo [3H]DASB (N,N-dimethyl-2-(2-amino-4-cyanophenylthio)benzylamine) binding from rat cortex and hippocampus, indicating that vilazodone occupies 5-HT transporters in vivo. Using in vivo microdialysis, vilazodone (10 mg/kg p.o.) was demonstrated to cause a 2-fold increase in extracellular 5-HT but no change in noradrenaline or dopamine levels in frontal cortex of freely moving rats. In contrast, administration of 8-OH-DPAT (0.3 mg/kg s.c.), either alone or in combination with a serotonin specific reuptake inhibitor (SSRI; paroxetine, 3 mg/kg p.o.), produced no increase in cortical 5-HT while increasing noradrenaline and dopamine 2 and 4 fold, resp. A 2-fold increase in extracellular 5-HT levels (but no change in noradrenaline or dopamine levels) was observed after combination of the 5-HT1A receptor antagonist, N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-N-(pyridinyl)cyclohexanecarboxamide (WAY-100635; 0.3 mg/kg s.c.) and paroxetine (3 mg/kg p.o.). In summary, vilazodone behaved as a high efficacy partial agonist at the rat hippocampal 5-HT1A receptors in vitro and occupied 5-HT transporters in vivo. In vivo vilazodone induced a selective increase in extracellular levels of 5-HT in the rat frontal cortex. This profile was similar to that seen with a 5-HT1A receptor antagonist plus an SSRI but in contrast to 8-OH-DPAT either alone or in combination with paroxetine.
IT **163521-12-8**, Vilazodone
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neurochem. evaluation of novel 5-HT1A receptor partial agonist and serotonin reuptake inhibitor vilazodone)
IT **163521-12-8**, Vilazodone
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neurochem. evaluation of novel 5-HT1A receptor partial agonist and serotonin reuptake inhibitor vilazodone)
RN 163521-12-8 HCAPLUS
CN 2-Benzofurancarboxamide, 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]- (CA INDEX NAME)

L48 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:1154699 HCAPLUS
DN 142:93856
TI Preparation of indolylbutylpiperazinylbenzofurancarboxamides as serotonin receptor ligands and/or serotonin reuptake inhibitors
IN **Heinrich, Timo**; Boettcher, Henning; **Schiemann, Kai**; Hoelzemann, Guenter; **Van Amsterdam, Christoph**; **Bartoszyk, Gerd**; **Laibrock, Joachim**; **Seyfried, Christoph**
PA **Merck** Patent GmbH, Germany
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO--2004113326	A1	20041229	2004WO-EP0005547	20040524 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE----10326939	A1	20050105	2003DE-100026939	20030616 <--
AU--2004249372	A1	20041229	2004AU-000249372	20040524 <--
CA-----2529299	A1	20041229	2004CA-002529299	20040524 <--
EP-----1633741	A1	20060315	2004EP-000734515	20040524 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LI, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN-----1805953	A	20060719	2004CN-080016700	20040524 <--
BR--2004011533	A	20060801	2004BR-000011533	20040524 <--
JP--2006527707	T	20061207	2006JP-000515787	20040524 <--
MX--2005013538	A	20060309	2005MX-000013538	20051213 <--
US-20070099933	A1	20070503	2005US-000560734	20051215 <--
PRAI 2003DE-100026939	A	20030616 <--		
2004WO-EP0005547	W	20040524 <--		

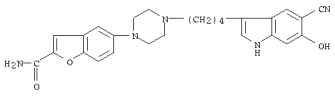
OS MARPAT 142:93856
GI



I

AB Title compds. [I; X = N, CH; R1-R3 = OH, OA, cyano, halo, COR4, CH2R4; R4 = OH, OA, NH2, NHB, NB2; Q = CH2, CO, CH; A, B = alkyl, alkoxy, alkenyl, alkoxyalkyl; m = 2-6; n = 0-4; dotted line = optional double bond], were prepared Thus, 5-[4-[4-(5-cyano-3-indolyl)butyl]-1-piperazinyl]benzofuran-2-carboxamide in Me2SO was treated dropwise with concentrate HCl under ice cooling followed by stirring for 10 h to give 5-[4-[4-(5-cyano-2-oxo-2,3-dihydro-1H-indol-3-yl)butyl]-1-piperazinyl]benzofuran-2-carboxamide as the dihydrochloride. The latter showed 5-HT1A receptor binding activity with IC50 = 1.7 nM and serotonin reuptake inhibitor activity with IC50 = 2.9 nM. I are useful as anxiolytics, antidepressants, neuroleptics, antihypertensives and/or for pos. influencing obsessive-compulsive behavior, sleeping disorders, tardive dyskinesia, learning disorders, age-related memory defects, eating disorders such as bulimia, and/or sexual dysfunction.
IT **714950-70-6P 816438-30-9P 816438-33-2P 816438-35-4P 816438-37-6P 816438-39-8P 816438-41-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

L48 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)
(Uses)
(prepn. of indolylbutylpiperazinylbenzofurancarboxamides as serotonin receptor ligands or reuptake inhibitors)
IT **163521-12-8 714950-88-6 765935-80-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of indolylbutylpiperazinylbenzofurancarboxamides as serotonin receptor ligands or reuptake inhibitors)
IT **714950-70-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indolylbutylpiperazinylbenzofurancarboxamides as serotonin receptor ligands or reuptake inhibitors)
RN 714950-70-6 HCAPLUS
CN 2-Benzofurancarboxamide, 5-[4-[4-(5-cyano-6-hydroxy-1H-indol-3-yl)butyl]-1-piperazinyl]- (CA INDEX NAME)



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:1154698 HCAPLUS
DN 142:93855
TI Preparation of indolylbutylpiperazinylbenzofurancarboxamides as serotonin reuptake inhibitors and/or serotonin receptor ligands.
IN **Heinrich, Timo**; Boettcher, Henning; **Schiemann, Kai**; Hoelzemann, Guenter; **Van Amsterdam, Christoph**; **Bartoszyk, Gerd**; **Laibrock, Joachim**; **Seyfried, Christoph**
PA **Merck** Patent GmbH, Germany; Van Amsterdam, Christoph
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO--2004113325	A1	20041229	2004WO-EP0005546	20040524 <--
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU--2004249371	A1	20041229	2004AU-000249371	20040524 <--
CA-----2529298	A1	20041229	2004CA-002529298	20040524 <--
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JP--2006527706	T	20061207	2006JP-000515786	20040524 <--
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US-20060160824	A1	20060720	2005US-000560737	20051215 <--
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OS MARPAT 142:93855
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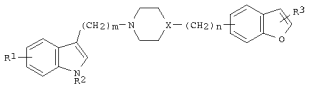
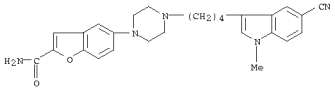


I

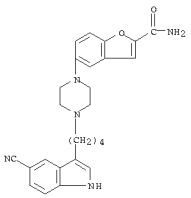
AB Title compds. [I; X = N, CH; R1, R3 = H, OH, OA, cyano, halo, COR4, CH2R4; R2 = H, (halo-substituted) alkyl, alkylaryl, alkylheteroaryl, heteroaryl; R4 = OH, OA, NH2, NHB, NB2; A, B = alkyl; m = 2-6; n = 0-4], were prepared Thus, 3-(4-chlorobutyl)-1H-indole-5-carbonitrile in THF was added to NaH in THF followed by stirring for 30 min., addition of MeI in THF, and stirring for 30 min. at room temperature to give N-methylated product, which was heated with 5-(piperazin-1-yl)benzofuran-2-carboxamide and Et3N in N-methylpyrrolidine at 120° for 4 h to give 5-[4-[4-(5-cyano-1-methyl-1H-indol-3-yl)butyl]piperazin-1-yl]benzofuran-2-carboxamide. The latter showed serotonin reuptake inhibitory activity with IC50 = 2.6 nM. I are useful as anxiolytics, antidepressants, neuroleptics, antihypertensives, and/or for pos. influencing obsessive compulsive disorders, sleep disorders, tardive dyskinesia, learning disorders, geriatric memory loss, bulimia, irritable bowel syndrome, and sexual dysfunction.

L48 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)
IT **816429-14-8P 816429-15-9P 816429-16-0P**
816429-17-1P 816429-18-2P 816429-19-3P
816429-20-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of indolylbutylpiperazinylbenzofurancarboxamides as serotonin reuptake inhibitors and/or serotonin receptor ligands)
IT **816429-21-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indolylbutylpiperazinylbenzofurancarboxamides as serotonin reuptake inhibitors and/or serotonin receptor ligands)
IT **816429-14-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of indolylbutylpiperazinylbenzofurancarboxamides as serotonin reuptake inhibitors and/or serotonin receptor ligands)
RN 816429-14-8 HCAPLUS
CN 2-Benzofurancarboxamide, 5-[4-[4-(5-cyano-1-methyl-1H-indol-3-yl)butyl]-1-piperazinyl]- (CA INDEX NAME)



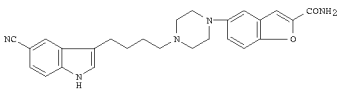
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:892421 HCAPLUS
DN 141:360593
TI Effects of systemic injections of Vilazodone, a selective serotonin reuptake inhibitor and serotonin 1A receptor agonist, on anxiety induced by predator stress in rats
AU Adamec, Robert; **Bartoszyk, Gerd D.**; Burton, Paul
CS Department of Psychology, Memorial University, St. John's, A1B 3X9, Can.
SO European Journal of Pharmacology (**2004**), 504(1-2), 65-77
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier B.V.
DT Journal
LA English
AB We examined the effect of Vilazodone, a selective serotonin reuptake inhibitor (SSRI) and serotonin 1A (5-HT1A) receptor agonist [Bartoszyk, G.D., Hegenbart, R., Ziegler, H., 1997. EMD 68843, a serotonin reuptake inhibitor with selective presynaptic 5-HT1A receptor agonistic properties. Eur. J. Pharmacol. 322, 147-153], on change in affect following predator stress. Vilazodone and vehicle injection (i.p.) occurred either 10 min after predator stress (prophylactic testing), or 90 min prior to behavioral testing for the effects of predator stress (therapeutic testing). Predator stress involved unprotected exposure of rats to a domestic cat. Behavioral effects of stress were evaluated with hole board, plus-maze, and acoustic startle tests 1 wk after stress. Predator stress increased anxiety-like behavior in the plus-maze and elevated response to acoustic startle. In prophylactic testing, Vilazodone affected stress potentiation of startle at doses above 5 mg/kg. Vilazodone increased stress elevation of startle at 10 mg/kg. Higher doses of Vilazodone (20 and 40 mg/kg) blocked stress potentiation of startle. In contrast, Vilazodone had no effect on stress potentiation of anxiety in the plus-maze. In therapeutic testing, Vilazodone increased stress elevation of startle at all doses. In contrast, therapeutic Vilazodone had no effect on stress potentiation of anxiety in the plus-maze. Taken together, the data suggest a prophylactic potential for Vilazodone in the treatment of changes in hypervigilance following severe stress.
IT **163521-12-8**, Vilazodone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of SSRI and serotonin 1A receptor agonist, Vilazodone,. on anxiety induced by predator stress in rats)
IT **163521-12-8**, Vilazodone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of SSRI and serotonin 1A receptor agonist, Vilazodone,. on anxiety induced by predator stress in rats)
RN 163521-12-8 HCAPLUS
CN 2-Benzofurancarboxamide, 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]- (CA INDEX NAME)



RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

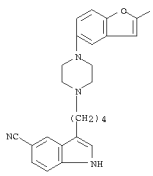
L48 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:641081 HCAPLUS
DN 141:314299
TI Synthesis and Structure-Activity Relationship in a Class of Indolebutylpiperazines as Dual 5-HT1A Receptor Agonists and Serotonin Reuptake Inhibitors
AU **Hainrich, Timo**; Boettcher, Henning; Gericke, Rolf; **Bartoszyk, Gerd D.**; Anzali, Soheila; **Seyfried, Christoph A.**; Greiner, Hartmut E.; **van Amsterdam, Christoph**
CS Preclinical Pharmaceutical Research, **Merck** KGaA, Darmstadt, 64293, Germany
SO Journal of Medicinal Chemistry (**2004**), 47(19), 4684-4692
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 141:314299
GI



I

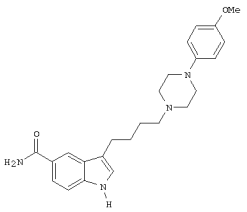
AB Systematic structural modifications of [(indolyl)alkyl](phenyl)piperazines led to improved selectivity and affinity within this class of 5-HT1A receptor agonists. Introduction of electron-withdrawing groups in position 5 on the indole group raises serotonin transporter affinity, and the cyano group proved to be the best substituent here. 5-Fluoro and 5-cyano substituted indoles show comparable results in in vitro and in vivo tests, and bioisosterism between these substituents was supported by calcn. of the mol. electrostatic potentials and dipole moments. Compds. showing promising in vitro data were further examined in ex vivo (p-chloroamphetamine assay) and in vivo (ultrasonic vocalization) tests. Optimization of the arylpiperazine moiety indicated that the 5-benzofuranyl-2-carboxamide was best suited to increase 5-HT transporter and 5-HT1A receptor affinity and to suppress D2 receptor binding. 5-[4-[4-(5-Cyano-3-indolyl)butyl]-1-piperazinyl]-2-benzofurancarboxamide (I; vilazodone, EMD 68843) was identified as a highly selective 5-HT1A receptor agonist [GTPγS, ED50 = 1.1 nM] with subnanomolar 5-HT1A affinity [IC50 = 0.2 nM] and as a subnanomolar 5-HT re-uptake inhibitor [RUI = 0.5 nM] showing a great selectivity to other GPCRs (e.g., D2, IC50 = 666 nM). I is a promising candidate for further investigation in the treatment of mood disorders (no data).
IT **163521-19-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (benzofuranyl)[(indolyl)alkyl]piperazine derivs. using [[(indolyl)alkyl]piperazinyl]benzofurancarboxylic acid as synthetic intermediate)
IT **163521-09-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (benzofuranyl)[(indolyl)butyl]piperazine derivs. using [[(indolyl)butyl]piperazinyl]benzofurancarboxylic acid ester as synthetic intermediate)
IT **765935-98-6P 765936-02-5P 765936-03-6P 765936-04-7P 765936-05-8P 765936-06-9P 765936-09-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [[(benzofuranyl)piperazinyl]butyl]indolecarbonitrile derivative and study of its activity as 5-HT1A receptor agonist and serotonin re-uptake inhibitor)

L48 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)
IT **163521-12-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of [[(cyanoindolyl)butyl]piperazinyl]benzofurancarboxamide derivative and study of its activity as 5-HT1A receptor agonist and serotonin re-uptake inhibitor)
IT **163521-08-2P**, Vilazodone hydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [[(cyanoindolyl)butyl]piperazinyl]benzofurancarboxamide derivative and study of its activity as 5-HT1A receptor agonist and serotonin re-uptake inhibitor)
IT **765935-77-1P 765935-79-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [[(indolyl)butyl]piperazinyl]benzofurancarbonitrile derivative and study of its activity as 5-HT1A receptor agonist and serotonin re-uptake inhibitor)
IT **765935-80-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [[(indolyl)butyl]piperazinyl]benzofurancarboxamide derivative and study of its activity as 5-HT1A receptor agonist and serotonin re-uptake inhibitor)
IT **163521-19-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (benzofuranyl)[(indolyl)alkyl]piperazine derivs. using [[(indolyl)alkyl]piperazinyl]benzofurancarboxylic acid as synthetic intermediate)
RN 163521-19-5 HCAPLUS
CN 2-Benzofurancarboxylic acid, 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]- (CA INDEX NAME)



RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

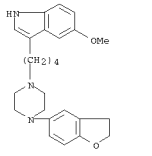
L48 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:641080 HCAPLUS
DN 141:295978
TI Indolebutylamines as Selective 5-HT1A Agonists
AU **Hainrich, Timo**; Boettcher, Henning; **Bartoszyk, Gerd D.**; Greiner, Hartmut E.; **Seyfried, Christoph A.**; **van Amsterdam, Christoph**
CS Preclinical Pharmaceutical Research, **Merck** KGaA, Darmstadt, 64293, Germany
SO Journal of Medicinal Chemistry (**2004**), 47(19), 4677-4683
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 141:295978
GI



I

AB A series of 1-[4-(indol-3-yl)butyl]-4-arylpiperazines, e.g., I, was prepared to identify highly selective and potent 5-HT1A agonists as potential pharmacol. tools in studies of mood disorders. The combination of structural elements (indole-alkyl-amine and aryl-piperazine) known to introduce 5-HT1A receptor affinity and the proper selection of substituents on the indole and aryl moieties led to compds. with high receptor specificity and affinity. In particular, the introduction of the Me ether or the unsubstituted carboxamide as substituents in position 5 of the indole guaranteed serotonergic 5-HT1A affinity compared to the unsubstituted analog. Para-substituted arylpiperazines decreased dopaminergic D2 binding and increased selectivity for the 5-HT1A receptor. Agonistic 5-HT1A receptor activity was confirmed in vivo in the ultrasonic vocalization test, and the results suggest that the introduction of the carboxamide residue led to better bioavailability than the corresponding Me ether. 3-{4-[4-(4-Carbamoylphenyl)piperazin-1-yl]butyl}-1H-indole-5-carboxamide was identified as a highly selective 5-HT1A receptor agonist [GTPγS, ED50 = 4.7 nM] with nanomolar 5-HT1A affinity [IC50 = 0.9 nM] and selectivity [D2, IC50 > 850 nM]. I was one of the most potent and selective 5-HT1A agonists known [5-HT1A, IC50 = 0.09 nM; D2, IC50 = 140 nM].
IT **163521-03-7P 765272-99-9P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, 5-HT1A and dopamine receptor affinity, and structure-activity relationship of indolebutylamine derivs.)
IT **765273-14-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation, 5-HT1A and dopamine receptor affinity, and structure-activity relationship of indolebutylamine derivs.)
IT **765272-76-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, 5-HT1A and dopamine receptor affinity, and structure-activity relationship of indolebutylamine derivs.)
IT **163521-03-7P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic

L48 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)
preparation); BIOL (Biological study); PREP (Preparation)
(prepn., 5-HT1A and dopamine receptor affinity, and structure-activity relationship of indolebutylamine derivs.)
RN 163521-03-7 HCAPLUS
CN 1H-Indole, 3-[4-[4-(2,3-dihydro-5-benzofuranyl)-1-piperazinyl]butyl]-5-methoxy- (CA INDEX NAME)



RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:525891 HCAPLUS
DN 141:89110
TI Preparation of piperazinylethylindolecarbonitriles as serotonin reuptake inhibitors and 5-HT1A/5-HT1B receptor ligands.
IN **Heinrich, Timo**; Boettcher, Henning; **Schiemann, Kai**; Hoelzemann, Guenter; **van Amsterdam, Christoph**; **Bartoszyk, Gerd**; **Laibrock, Joachim**; **Seyfried, Christoph**
PA **Merck** Patent GmbH, Germany
SO Ger. Offen., 23 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE----10259244	A1	20040701	2002DE-100059244	20021217 <--
CA-----2510169	A1	20040701	2003CA-002510169	20031127 <--
WO--2004054972	A1	20040701	2003WO-EP0013374	20031127 <--
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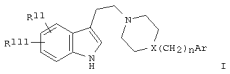
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU--2003298145	A1	20040709	2003AU-000298145	20031127 <--
EP-----1572646	A1	20050914	2003EP-000795848	20031127 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR--2003017422	A	20051108	2003BR-000017422	20031127 <--
CN-----1729173	A	20060201	2003CN-080106737	20031127 <--
JP---2006511522	T	20060406	2004JP-000559727	20031127 <--
MX---2005006385	A	20050829	2005MX-000006385	20050614 <--
US--20060122191	A1	20060608	2005US-000539516	20050617 <--
ZA---2005005684	A	20060426	2005ZA-000005684	20050714 <--
PRAI 2002DE-100059244	A	20021217 <--		
2003WO-EP0013374	W	20031127 <--		

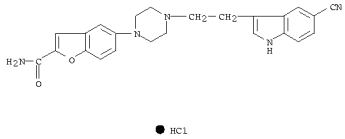
OS MARPAT 141:89110
GI



I

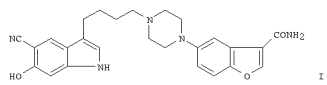
AB Title compds. [I; R11, R111 = H, cyano, halo, A, OA, OH, COR2, CH2R2; R2 = OH, OA, NH2, NHA, NA2; A = (fluoro-substituted) alkyl optionally interrupted by O, S, CH:CH; Ar = (partially or completely saturated) (substituted) mono- or polycyclic carbo- or heterocyclyl; n = 0-4], were prepared Thus, 3-(2-chloroeth-1-yl)-1H-indole-5-carbonitrile (preparation given), 1-(2,3-dihydrobenzo[1,4]-dioxin-5-yl)piperazine, ethyldiisopropylamine, and N-methylpyrrolidinone were heated together at 120° for 12 h to give 3-[2-[4-(2,3-dihydrobenzo[1,4]dioxin-5-yl)piperazin-1-yl]ethyl]-1H-indole-5-carbonitrile. The latter showed SSRI, 5-HT1A, and 5-HT1B receptor activity at 11 nM, 17 nM, and 11 nM, resp.
IT **714953-92-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinylethylindolecarbonitriles as serotonin reuptake inhibitors and receptor ligands)

L48 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)
IT **714953-92-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinylethylindolecarbonitriles as serotonin reuptake inhibitors and receptor ligands)
RN 714953-92-1 HCAPLUS
CN 2-Benzofurancarboxamide, 5-[4-[2-(5-cyano-1H-indol-3-yl)ethyl]-1-piperazinyl]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

L48 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:346288 HCAPLUS
DN 141:88987
TI A new synthesis of indole 5-carboxylic acids and 6-hydroxy-indole-5-carboxylic acids in the preparation of an o-hydroxylated metabolite of vilazodone
AU **Heinrich, Timo**; Boettcher, Henning
CS Preclinical Pharmaceutical Research, **Merck** KGaA, Darmstadt, 64293, Germany
SO Bioorganic & Medicinal Chemistry Letters (**2004**), 14(10), 2681-2684
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science B.V.
DT Journal
LA English
OS CASREACT 141:88987
GI



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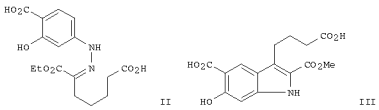
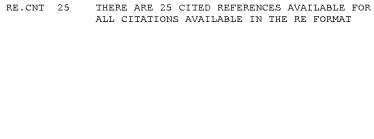


II III

AB A major metabolite of the potential antidepressant vilazodone formed in rat, dog, monkey and human liver microsomes is 5-[4-[4-(5-cyano-6-hydroxy-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofurancarboxamide (I). For the construction of the salicyl-like substituted indole a synthesis of carmoxirole was adapted using Japp-Klingemann-type Fischer-indole synthesis protocols. The reaction of 4-amino-2-hydroxybenzoic acid with 2-oxocyclohexanecarboxylic acid Et ester gave 4-[[5-carboxy-1-(ethoxycarbonyl)pentylidene]hydrazino]-2-hydroxybenzoic acid (II). The Japp-Klingemann reaction of II gave a 6:1 mixture of 5-carboxy-6-hydroxy-2-(methoxycarbonyl)-1H-indole-3-butanoic acid (III) and its 4-hydroxy isomer, 5-carboxy-4-hydroxy-2-(methoxycarbonyl)-1H-indole-3-butanoic acid. Functional group interconversion of carboxylic acid via carboxamide into cyanide was performed for III. The synthesis of carmoxirole [i.e., 3-[4-(3,6-dihydro-4-phenyl-1(2H)-pyridinyl)butyl]-1H-indole-5-carboxylic acid] was also reported using this Japp-Klingemann-type Fischer-indole synthesis protocol.
IT **714950-88-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of vilazodone metabolite via Japp-Klingemann-type Fischer indole synthesis of 2,5-dicarboxy-6-hydroxy-1H-indole-3-butanoate from [[carboxy(ethoxycarbonyl)pentylidene]hydrazino](hydroxy)benzoate intermediate)
IT **163521-12-8DP**, Vilazodone, metabolites
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of vilazodone metabolite via Japp-Klingemann-type Fischer indole synthesis of 2,5-dicarboxy-6-hydroxy-1H-indole-3-butanoate from [[carboxy(ethoxycarbonyl)pentylidene]hydrazino](hydroxy)benzoate intermediate)
IT **714950-70-6P**, 5-[4-[4-(5-Cyano-6-hydroxy-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofurancarboxamide
RL: SPN (Synthetic preparation); PREP (Preparation)
(vilazodone metabolite; preparation of vilazodone metabolite via Japp-Klingemann-type Fischer indole synthesis of

L48 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)
2,5-dicarboxy-6-hydroxy-1H-indole-3-butanoate from [[carboxy(ethoxycarbonyl)pentylidene]hydrazino](hydroxy)benzoate intermediate)
IT **714950-88-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of vilazodone metabolite via Japp-Klingemann-type Fischer indole synthesis of 2,5-dicarboxy-6-hydroxy-1H-indole-3-butanoate from [[carboxy(ethoxycarbonyl)pentylidene]hydrazino](hydroxy)benzoate intermediate)
RN 714950-88-6 HCAPLUS
CN 2-Benzofurancarboxamide, 5-[4-[4-[5-cyano-6-[(methylsulfonyl)oxy]-1H-indol-3-yl]butyl]-1-piperazinyl]- (CA INDEX NAME)



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2003:837073 HCAPLUS
DN 139:337888
TI Preparation of indole-3-carbonitriles as excitatory amino acid antagonists for the treatment of neurodegenerative diseases
IN Schadt, Oliver; Boettcher, Henning; **Leibrock, Joachim**; **Schiemann, Kai**; **Heinrich, Timo**; Hoelzemann, Guenter; **Van Amsterdam, Christoph**; **Bartoszyk, Gerd**; **Seyfried, Christoph**
PA **Merck** Patent G.m.b.H., Germany
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO--2003087086	A2	20031023	2003WO-EP0003806	20030411 <--
WO--2003087086	A3	20040722		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE----10217006	A1	20031106	2002DE-100017006	20020416 <--
CA-----2482655	A1	20031023	2003CA-002482655	20030411 <--
AU--2003224064	A1	20031027	2003AU-000224064	20030411 <--
EP-----1497279	A2	20050119	2003EP-0007720455	20030411 <--
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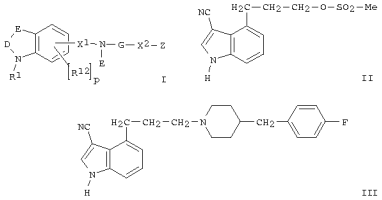
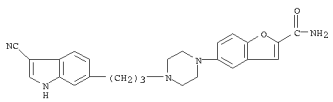
JP--2005523310	T	20050804	2003JP-000584042	20030411 <--
US-20050153980	A1	20050714	2004US-000511155	20041014 <--
US-20090054459	A1	20090226	2008US-000245416	20081003 <--
PRAI 2002DE-100017006	A	20020416	<--	
2003WO-EP0003806	W	20030411	<--	
2004US-000511155	A3	20041014		

OS MARPAT 139:337888
GI



AB Title compds. I [R1 = H, A, SO2A; A = alkyl, alkoxyalkyl; D-E = R2C=CR4, R2R3C-CR4R5; R2, R3, R4, R5 = H, A, cycloalkyl, etc.; X1 = (CHR7)g, (CHR7)h-Q-(CHR8)k; Q = O, S, NR6, etc.; R6 = H, A, cycloalkyl; R7, R8, R12 = definition as given for R2-R5; g = 1-6; h, k = 0-6; p = 0-3; E = H, A,

L48 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)
cycloalkyl, etc.; G = (un)substituted alkylene; E and G together form (un)substituted mono or bicyclic heterocycle; X2 = definition as given for X1; Z = H, (un)substituted arom. carbocyle] and their pharmaceutically acceptable salts and formulations were prepd. For example, N-alkylation of 4-(4-fluorobenzyl)piperideine with methanesulfonic ester II, e.g., prepd. from indole-4-carboxylic acid Me ester in 7-steps, afforded the hydrochloride salt of indole-3-carbonitrile III after work-up. Compds. I are claimed useful as excitatory amino acid antagonists (no data provided) and as 5-HT reuptake inhibitors.
IT **615569-38-5P 615569-40-9P 615569-41-0P**
615569-77-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of indole-3-carbonitriles as excitatory amino acid antagonists for the treatment of neurodegenerative diseases)
IT **615569-38-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of indole-3-carbonitriles as excitatory amino acid antagonists for the treatment of neurodegenerative diseases)
RN 615569-38-5 HCAPLUS
CN 2-Benzofurancarboxamide, 5-[4-[3-(3-cyano-1H-indol-6-yl)propyl]-1-piperazinyl]- (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2002:977808 HCAPLUS
DN 138:44671
TI Polymorphic forms of 1-'4-(5-cyanoindol-3-yl)butyl-4-(2-carbamoylbenzofuran-5-yl)piperazine hydrochloride
IN Bathe, Andreas; Helfert, Bernd; Neuenfeld, Steffen; Kniel, Heike; Bartels, Matthias; Rudolph, Susanne; Boettcher, Henning
PA **Merck** Patent G.m.b.H., Germany
SO PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

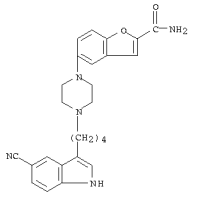
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO--2002102794	A2	20021227	2002WO-EP0006153	20020605 <--
WO--2002102794	A3	20030220		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA-----2451028	A1	20021227	2002CA-002451028	20020605 <--
AU--2002320822	A1	20030102	2002AU-000320822	20020605 <--
AU--2002320822	B2	20071115		
EP-----1397357	A2	20040317	2002EP-0007546277	20020605 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE---200400019	A	20040415	2004EE-000000019	20020605 <--
HU--2004000236	A2	20040628	2004HU-000000236	20020605 <--
CN-----1516699	A	20040728	2002CN-000812226	20020605 <--
CN---100384841	C	20080430		
BR--2002010495	A	20040817	2002BR-000010495	20020605 <--
JP--2004534803	T	20041118	2003JP-000506267	20020605 <--
NZ------530642	A	20060929	2002NZ-000530642	20020605 <--
RU-----2303598	C2	20070727	2004RU-000100824	20020605 <--
CN---101139345	A	20080312	2007CN-0101802229	20020605 <--
MX--2003011723	A	20040319	2003MX-000011723	20031216 <--
US-20040147528	A1	20040729	2003US-000481270	20031219 <--
US-----7381726	B2	20080603		
IN---200400031	A	20060407	2004IN-000000031	20040109 <--
ZA--2004000329	A	20050415	2004ZA-000000329	20040115 <--
HK-----1066003	A1	20081031	2004HK-000108857	20041110 <--
US-20090023749	A1	20090122	2008US-000110704	20080428 <--
PRAI 2001EP-000113647	A	20010619	<--	
2002CN-000812226	A3	20020605	<--	
2002WO-EP0006153	W	20020605	<--	
2003US-000481270	A3	20031219	<--	

AB The invention relates to new crystalline modifications of the hydrochloride salt of 1-[4-(5-cyanoindol-3-yl)butyl]-4-(2-carbamoyl-benzofuran-5-yl)-piperazine, crystalline modification of the dihydrochloride of 1-[4-(5-cyanoindol-3-yl)butyl]-4-(2-carbamoylbenzofuran-5-yl]piperazine and amorphous 1-[4-(5-cyanoindol-3-yl)butyl]-4-(2-carbamoyl-benzofuran-5-yl)piperazine-HCl (I) which are suitable in particular for the preparation of solid pharmaceuticals for the treatment or prevention of depressive disorders, anxiety disorders, bipolar disorders, mania, dementia, substance-related disorders, sexual dysfunctions, eating disorders, obesity, fibromyalgia, sleeping disorders, psychiatric disorders, cerebral infarction, tension, for the therapy of side-effects in the treatment of hypogonadism, secondary amenorrhea, premenstrual syndrome and undesired puerperal lactation. Thus, to a solution of 1-[4-(5-cyanoindol-3-yl)butyl]-4-(2-carbamoylbenzofuran-5-yl]piperazine in THF was added HCl. The I hydrate obtained was dried at 85-90° to give I which was characterized by spectral properties.
IT **478917-86-1P 478917-87-2P 478917-88-3P**
478917-89-4P 478917-90-7P 478917-92-9P
478917-93-0P 478917-94-1P 478917-95-2P
478917-96-3P 478917-97-4P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of polymorphic forms of (cyanoindolyl)butylcarbamoylbenzofuranylpiperazine hydrochloride)

L48 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)
IT **163521-08-2P 478917-91-8P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polymorphic forms of (cyanoindolyl)butylcarbamoylbenzofuranylpiperazine hydrochloride)
IT **478917-86-1P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of polymorphic forms of (cyanoindolyl)butylcarbamoylbenzofuranylpiperazine hydrochloride)
RN 478917-86-1 HCAPLUS
CN 2-Benzofurancarboxamide, 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-, compd. with 2-propanone (1:?) (CA INDEX NAME)

CM 1

CRN 163521-08-2
CMF C26 H27 N5 O2 . Cl H



● HCl

CM 2

CRN 67-64-1
CMF C3 H6 O

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2002:714050 HCAPLUS
DN 137:232676
TI Preparation of 5-piperazinylbenzofuran-2-carboxamides as 5-HT1A agonists and 5-HT reuptake inhibitors
IN Dorsch, Dieter; Boettcher, Henning; **Van Amsterdam, Christoph**; Rautenberger, Wilfried; **Bartoszyk, Gerd**
PA **Merck** Patent Gmbh, Germany
SO Ger. Offen., 14 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE----10112151	A1	20020919	2001DE-100012151	20010314 <--
CA-----2440726	A1	20021024	2002CA-002440726	20020227 <--
WO--2002083666	A1	20021024	2002WO-EP0002093	20020227 <--
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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EP-----1368346	A1	20031210	2002EP-000729940	20020227 <--
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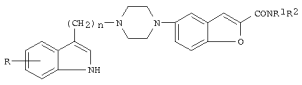
HU--2003003449	A2	20040128	2003HU-000003449	20020227 <--
HU--2003003449	A3	20050228		
BR--2002008040	A	20040225	2002BR-000008040	20020227 <--
CN-----1494543	A	20040505	2002CN-000805813	20020227 <--
CN-----1244578	C	20060308		
JP--2004527536	T	20040909	2002JP-000581421	20020227 <--
MX--2003008140	A	20031212	2003MX-000008140	20030909 <--
US-20050075269	A1	20050407	2003US-000471584	20030912 <--
US-----7244846	B2	20070717		
ZA---2003007966	A	20050113	2003ZA-000007966	20031013 <--
IN---200301319	A	20060310	2003IN-000001319	20031014 <--
PRAI 2001DE-100012151	A	20010314	<--	
2002WO-EP0002093	W	20020227	<--	

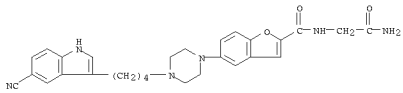
OS MARPAT 137:232676
GI



I

AB Title compds. [I; R = H, OH, OA, cyano, halo, CH2R3; R1 = (A-substituted) cycloalkyl, (branched) (substituted) (O-, S-, CH:CH-, C.tplbond.C-interrupted) alkyl; R2 = H, A, R1; or NR1R2 = 3-7 membered saturated (substituted) heterocyclyl; R3 = OH, OA, N(R4)2; R4 = H, A; A = (branched) (fluorinated) (O-, S-, CH:CH-interrupted) C1-6 alkyl; n = 2-5] and salts thereof were prepared as 5-HT1A agonists and 5-HT reuptake inhibitors (no data). Thus, a mixture of 200 mg 5-[4-(4-[5-cyano-1H-indol-3-yl]butyl)piperazin-1-yl]benzofuran-2-carboxylic acid, 50 mg NH2CH2CONH2.HCl, N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (EDC), and hydroxybenzotriazole hydrate (HOBT) in DMF was stirred for 18 h at room temperature to give 2-(5-[4-(4-[5-cyano-1H-indol-3-yl]butyl)piperazin-1-

L48 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)
yl]benzofuranyl)-N-(carbamoylmethyl]amide.
IT **459124-98-2P 459124-99-3P 459125-00-9P 459125-01-0P 459125-02-1P 459125-03-2P 459125-04-3P 459125-05-4P 459125-06-5P 459125-07-6P 459125-08-7P 459125-09-8P 459125-10-1P 459125-11-2P 459125-12-3P 459125-13-4P 459125-14-5P 459125-15-6P 459125-16-7P 459125-17-8P 459125-18-9P 459125-19-0P 459125-20-3P 459125-21-4P 459125-22-5P 459125-23-6P 459125-24-7P 459125-25-8P 459125-26-9P 459125-27-0P 459125-28-1P 459125-29-2P 459125-30-5P 459125-31-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinylbenzofurancarboxamides as 5-HT1A agonists and S-HT reuptake inhibitors)
IT **163521-19-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazinylbenzofurancarboxamides as 5-HT1A agonists and S-HT reuptake inhibitors)
IT **459124-98-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinylbenzofurancarboxamides as 5-HT1A agonists and S-HT reuptake inhibitors)
RN 459124-98-2 HCAPLUS
CN 2-Benzofurancarboxamide, N-(2-amino-2-oxoethyl)-5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]- (CA INDEX NAME)



L48 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2002:391537 HCAPLUS
DN 136:380124
TI Veterinary use of combined 5-HT1a agonists and serotonin reuptake inhibitors for the treatment of traumatic and compulsive disorders associated with behavioral stressors
IN **Bartoszyk, Gerd**
PA **Merck** Patent Gmbh, Germany
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO--2002040024	A1	20020523	2001WO-EP0011952	20011016 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA-----2428511	A1	20020523	2001CA-002428511	20011016 <--
AU--2002015027	A	20020527	2002AU-000015027	20011016 <--
EP-----1333832	A1	20030813	2001EP-000983555	20011016 <--
EP-----1333832	B1	20071128		
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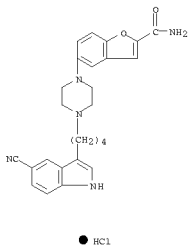
HU--2003002751	A2	20031128	2003HU-000002751	20011016 <--
HU--2003002751	A3	20070628		
JP--2004513924	T	20040513	2002JP-000542397	20011016 <--
CN-----1222291	C	20051012	2001CN-000818859	20011016 <--
AU--2002215027	B2	20061005	2002AU-000215027	20011016 <--
RU-----2288719	C2	20061210	2003RU-000115431	20011016 <--
ES-----2296820	T3	20080501	2001ES-000983555	20011016 <--
MX--2003004166	A	20030922	2003MX-000004166	20030512 <--
NO--2003002148	A	20030513	2003NO-000002148	20030513 <--
US-20040082594	A1	20040429	2003US-000416573	20030513 <--
IN---200300745	A	20050204	2003IN-000000745	20030610 <--
ZA---2003004606	A	20040913	2003ZA-000004606	20030612 <--
HK-----1060697	A1	20060707	2004HK-000103692	20040525 <--
PRAI 2000EP-000124815	A	20001114	<--	
2001WO-EP0011952	W	20011016	<--	

AB The invention discloses the use of combined selective serotonin (5-HT) reuptake inhibitors (SSRIs) and 5-HT1A receptor agonists, in particular 1-[4-(5-cyanoindol-3-yl)butyl]-4-(2-carbamoyl-benzofuran-5-yl)-piperazine, or a physiol. acceptable salt thereof, or 3-[4-(4-(4-cyano-phenyl)-piperazin-1-yl)-butyl]-1H-indole-5-carbonitrile, or a physiol. acceptable salt thereof, for the manufacture of a medicament for use in veterinary medicine for the treatment or prophylaxis of self-directed traumatic disorders associated with behavioral stressors and compulsive disorders associated with behavioral stressors.
IT **163521-08-2 163521-12-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(veterinary use of combined 5-HT1a agonists and serotonin reuptake inhibitors for treatment of traumatic and compulsive disorders associated with behavioral stressors)
IT **163521-08-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(veterinary use of combined 5-HT1a agonists and serotonin reuptake inhibitors for treatment of traumatic and compulsive disorders associated with behavioral stressors)
RN 163521-08-2 HCAPLUS
CN 2-Benzofurancarboxamide, 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-, hydrochloride (1:1) (CA INDEX NAME)

L48 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)



● HCl

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2002:391504 HCAPLUS
DN 136:380120
TI Novel use of combined 5-HT1a agonists and selective serotonin reuptake inhibitors
IN **Bartoszyk, Gerd**; Sedman, Ewen
PA **Merck** Patent Gmbh, Germany
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO--2002039989	A1	20020523	2001WO-EP0012686	20011102 <--
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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	AU--2002021803	A	20020527	2002AU-000021803	20011102 <--
	EP-----1335716	A1	20030820	2001EP-000996368	20011102 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR--2001015434	A	20031007	2001BR-000015434	20011102 <--
	JP--2004513916	T	20040513	2002JP-000542364	20011102 <--
	HU--2004000504	A2	20040628	2004HU-000000504	20011102 <--
	HU--2004000504	A3	20060228		
	CN-----1541093	A	20041027	2001CN-000819111	20011102 <--
	AU--2002221803	B2	20070215	2002AU-000221803	20011102 <--
	RU-----2302243	C2	20070710	2003RU-000116893	20011102 <--
	MX--2003004341	A	20030819	2003MX-000004341	20030516 <--
	NO--2003002248	A	20030519	2003NO-000002248	20030519 <--
	US-20040014771	A1	20040122	2003US-000432047	20030519 <--
	US-----7479492	B2	20090120		
	IN---2003007778	A	20060317	2003IN-000007778	20030613 <--
	ZA--2003004757	A	20040920	2003ZA-000004757	20030619 <--
PRAI	2000EP-000125409	A	20001120	<--	
	2001WO-EP0012686	W	20011102	<--	

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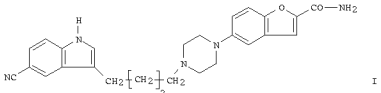
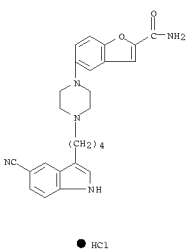


I

AB The present invention relates to the use of compds. being combined selective serotonin (5-HT) reuptake inhibitors (SSRIs) and 5-HT1A receptor agonists, in particular of I or a physiol. acceptable salt thereof or 3-[4-[4-(4-cyanophenyl)piperazin-1-yl]butyl]-1H-indole-5-carbonitrile or a physiol. acceptable salt thereof, for the manufacture of a medicament for the treatment of chronic pain disorders or in treating other conditions where there is hyper-sensitization to painful signals, hyperalgesia, allodynia, enhanced pain perception, and enhanced memory of pain, as well as for the treatment of irritable bowel syndrome (IBS). I-HCl reduced writhing in mice at 30 mg/kg orally by 82% in pain-relieving acute analgetic property tests.
IT **163521-08-2 163521-12-8**

L48 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined 5-HT1a agonists and selective serotonin reuptake inhibitors as analgesics)
IT **163521-08-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined 5-HT1a agonists and selective serotonin reuptake inhibitors as analgesics)
RN 163521-08-2 HCAPLUS
CN 2-Benzofurancarboxamide, 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2002:293443 HCAPLUS
DN 136:319370
TI Use of defined substances that bind to the sigma receptor for combating sarcoma and carcinoma
IN **Van Amsterdam, Christoph**
PA **Merck** Patent Gmbh, Germany
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO--2002030422	A1	20020418	2001WO-EP0011710	20011011 <--
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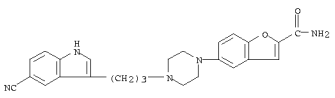
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE----10050236	A1	20020425	2000DE-10050236	20001011 <--
	AU--2002010527	A	20020422	2002AU-000010527	20011011 <--
PRAI	2000DE-100050236	A	20001011	<--	
	2001WO-EP0011710	W	20011011	<--	

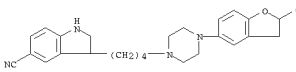
AB The invention relates to the use of a compound, selected from 3-[4-(4-phenyl-1,2-3,6-tetrahydro-1-pyridyl)butyl]indole-5-ol, 1-(2-(bis(4-fluorophenyl)methoxy)ethyl)-4-(3-phenyl-propyl)piperazine, 1-(4-hydroxyphenyl)-2-(4-benzyl-1-piperidinyl]propanol, 3-(4-((3S)-3-benzyl-1-piperidyl)butyl]indole-5-carbonitrile, 3-(4-((3R)-3-benzyl-1-piperidyl)butyl]indole-5-carbonitrile, 6-(4-(4-(5-fluoro-3-indolyl)butyl)-1-piperazinyl)-2H-1-benzopyrane-2-one, (5S)-(-)-5-[4-(4-aminobenzyl)-1-piperidylmethyl]-3-(4-ethylphenyl)oxazolidine-2-one, 6-3-[4-(2,4-difluorobenzyl)-1-piperidyl]-1-oxopropyl-2,3-dihydrobenzoxazole-2-one. 3-(4-(3-(4-Fluorophenyl-hydroxymethyl)piperido-1-yl)butyl)-5-indole-carbonitrile, 2-(4-[3-(5H-dibenz[b,f]azepine-5-yl)propyl]-1-piperazinyl)ethanol, 1-[2-(3,4-dimethoxyphenyl)ethyl]-4-(3-phenylpropyl]piperazine, (5S)-(-)-5-(4-benzyl-1-piperidylmethyl)-3-(4-chlorophenyl)oxazolidine-2-one, 6-3-[4-(4-fluorobenzyl)-1-piperidyl]-2-methylpropionyl-2,3-dihydrobenzoxazole-2-one, (1R,2S)-(+)-4-(3-(4-benzyl-piperidino-1-yl]-1-hydroxy-2-methyl-propyl)phenol, (E)-4-(3-(4-benzyl-piperidino-1-yl)-2-methyl-propenyl)phenol, 3-(4-(4-(2,1,3-benzothiadiazole-5-yl)-1-piperazinyl)butyl]indole-5-carbonitrile, 6-(3-(4-(4-fluorobenzyl)-1-piperidyl)-2-propenyl)-2,3-dihydrobenzoxazole-2-one, 3-(4-trifluoromethylphenoxymethyl)pyrrolidine, 6-3-[4-(4-fluorobenzyl)-2-piperidyl]-propionyl-3H-benzothiazole-2-one, 4-[3-(4-(4-fluorobenzyl)piperidino-1-yl]propoxyphenol, [2-(4-methoxy-3-phenethyloxy-phenyl]ethyl]dipropyl-amine. (1S,5R)-3-(2-(2-adamantyl)ethyl)-1,8,8-trimethyl-3-azabicyclo[3.2.1]octane, 6-3-[4-(2,4-difluorobenzyl)piperidino-1-yl]propionyl-3H-benzothiazole-2-one, 1-1-[2-(4-fluoro-phenyl)ethyl]piperidino-4-ylindane-1-ol, 1-[2-(4-fluoro-phenyl)ethyl]-4-(naphthalino-2-sulfinyl)piperidine, 1-(indole-4-yl)-4-(4-(4-fluorophenyl)butyl]piperazine, 3-(4-(2-(2-phenyl-ethyl)-1-piperidyl)-1-butyl)indole, 2-[4-(4-(3-indolyl)butyl)-1-piperazinyl]benzonitrile, etc., or the corresponding acids, bases, or salts, which may be used as σ-receptor ligands for treating carcinoma or sarcoma.
IT **411242-85-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substances that bind to sigma receptor for combating sarcoma and carcinoma)
IT **411242-85-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substances that bind to sigma receptor for combating sarcoma and carcinoma)
RN 411242-85-8 HCAPLUS
CN 2-Benzofurancarboxamide, 5-[4-[3-(5-cyano-1H-indol-3-yl]propyl]-1-

L48 ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)
piperazinyl]- (CA INDEX NAME)



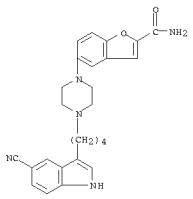
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2001:454453 HCAPLUS
DN 135:282632
TI Studies comparing in vivo:in vitro metabolism of three pharmaceutical compounds in rats, dogs, monkeys, and humans [by] using cryopreserved hepatocytes, microsomes, and collagen-gel-immobilized hepatocyte cultures
AU Hewitt, Nicola J.; Buhring, Karl-Ulrich; Dasenbrock, Johannes; Haunschild, Jutta; Ladstetter, Bernhard; Utesch, Dietmar
CS Institute of Toxicology, **Merck** KGaA, Darmstadt, D-64271, Germany
SO Drug Metabolism and Disposition (**2001**), 29(7), 1042-1050
CODEN: DMDSAI; ISSN: 0090-9556
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB The in vivo metabolism of EMD68843, EMD96785, and EMD128130 was compared in fresh and cryopreserved hepatocyte (CPH) suspensions and microsomes from rat, dog, monkey, and human livers and in fresh human and rat hepatocyte collagen-gel-immobilized cultures (GICs). Half of the major in vivo metabolites were produced by phase 1 metabolism (hydroxylation, oxidation, hydrolysis, N-dealkylation) and half by phase 2 metabolism (mostly glucuronidation but also sulfation and glycine conjugation). The identities and percentages of phase 1 and 2 metabolites of each compound produced in hepatocytes compared well with those in each species in vivo. Glucuronidation was more extensive in GICs than in CPHs. In contrast, CPHs, but not GICs, produced sulfate metabolites. Microsomes (supplemented with NADPH only) produced most of the phase 1 but no phase 2 metabolites. Metabolism by CPHs was the same as that by fresh hepatocyte suspensions. Discrete species differences in metabolism were detected in CPHs and microsomes. The cytochrome P 450 and glucuronosyl S-transferase contents of CPHs did not account for the species differences in the percentage of phase 1 and 2 metabolites or the rate of disappearance of the parent compds. in these cells. These data show a good correlation between major metabolites formed in vivo and in vitro. CPHs and GICs, unlike microsomes, carried out sequential phase 1 and 2 metabolism. Each in vitro system has its own advantages; however, for short-term metabolism studies CPHs may be more useful, since they are readily available, easier and quicker to prepare than GICs, and have more comprehensive enzyme systems than microsomes.
IT **364064-12-0 364064-14-2 364064-15-3**
364070-35-9 364070-36-0
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(in vivo vs. in vitro metabolism of EMD 68843 in rats, dogs, monkeys, and humans by cryopreserved hepatocytes, microsomes, and collagen-gel-immobilized hepatocyte cultures as determined by formation of)
IT **364064-12-0**
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(in vivo vs. in vitro metabolism of EMD 68843 in rats, dogs, monkeys, and humans by cryopreserved hepatocytes, microsomes, and collagen-gel-immobilized hepatocyte cultures as determined by formation of)
RN 364064-12-0 HCAPLUS
CN 2-Benzofurancarboxylic acid, 5-[4-[4-(5-cyano-2,3-dihydro-1H-indol-3-yl)butyl]-1-piperazinyl]-2,3-dihydro- (CA INDEX NAME)



RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2001:164199 HCAPLUS
DN 135:441
TI Systemic EMD 68843 injections reduce anxiety in the shock-probe, but not the plus-maze test
AU Treit, D.; Degroot, A.; Kashluba, S.; **Bartoszyk, G. D.**
CS Department of Psychology, University of Alberta, Edmonton, AB, T6G 2E9, Can.
SO European Journal of Pharmacology (**2001**), 414(2/3), 245-248
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB Selective serotonin (5-hydroxytryptamine; 5-HT) reuptake inhibitors and 5-HT1A receptor agonists are believed to reduce anxiety. In the present study we examined the effects of injections of 5-[4-[4-(5-cyano-3-indolyl)-butyl]-1-piperazinyl]-benzofuran-2-carboxamide hydrochloride (EMD 68843), a 5-HT1A receptor agonist and selective 5-HT reuptake inhibitor, in two animal models of anxiety, plus-maze and shock-probe. Rats received i.p. injections of vehicle, diazepam (2.5 mg/kg), or EMD 68843 (10, 20, or 40 mg/kg) 1 h prior to testing. Diazepam at the single dose tested and EMD 68843 dose-dependently (significantly at 20 and 40 mg/kg) reduced burying in shock-probe. However, only diazepam significantly increased open arm exploration in the plus-maze. Therefore, EMD 68843 has task specific anxiolytic properties.
IT **163521-12-8**, EMD 68843
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(systemic EMD 68843 injections reduce anxiety in shock-probe, but not plus-maze test)
IT **163521-12-8**, EMD 68843
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(systemic EMD 68843 injections reduce anxiety in shock-probe, but not plus-maze test)
RN 163521-12-8 HCAPLUS
CN 2-Benzofurancarboxamide, 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]- (CA INDEX NAME)



RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 2000:861478 HCAPLUS
DN 134:32976
TI Novel use of cyanoindolylbutyl(carbamoylbenzofuranyl)-piperazine and its physiologically acceptable salts for treatment of anxiety and related disorders
IN **Bartoszyk, Gerd; Seyfried, Christoph; Van Amsterdam, Christoph; Bottcher, Henning**; Sedman, Ewen
PA **Merck** Patent G.m.b.H., Germany
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI WO--2000072832	A2	20001207	2000WO-EP0004376	20000516	<--
WO--2000072832	A3	20011220			
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
TW------518218	B	20030121	1999TW-088119882	19991115	<--
CA------2372668	A1	20001207	2000CA-002372668	20000516	<--
CA------2615271	A1	20001207	2000CA-002615271	20000516	<--
EP------1185272	A2	20020313	2000EP-000935031	20000516	<--
EP------1185272	B1	20040407			
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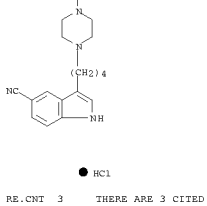
BR--2000010948	A	20020423	2000BR-000010948	20000516	<--
TR---200103361	T2	20020521	2001TR-000003361	20000516	<--
CN------1361692	A	20020731	2000CN-000808135	20000516	<--
CN------1198618	C	20050427			
HU--2002001275	A2	20020828	2002HU-000001275	20000516	<--
HU--2002001275	A3	20040428			
JP---2003500441	T	20030107	2000JP-000620944	20000516	<--
AU------771778	B2	20040401	2000AU-000050663	20000516	<--
AT------263564	T	20040415	2000AT-000935031	20000516	<--
EP------1410800	A1	20040421	2004EP-000001441	20000516	<--
EP------1410800	B1	20060823			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY					
PT------1185272	T	20040831	2000PT-000935031	20000516	<--
RU------2237477	C2	20041010	2001RU-000133342	20000516	<--
ES------2219342	T3	20041201	2000ES-000935031	20000516	<--
US------6900212	B1	20050531	2001US-000979922	20000516	<--
CZ------295623	B6	20050914	2001CZ-000004226	20000516	<--
CN------1679577	A	20051012	2005CN-010054417	20000516	<--
AT------337008	T	20060915	2004AT-000001441	20000516	<--
EP------1736158	A2	20061227	2006EP-000017231	20000516	<--
EP------1736158	A3	20070103			
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, LT, LV, RO, SI					
ES------2271707	T3	20070416	2004ES-000001441	20000516	<--
IL------146707	A	20070603	2000IL-000146707	20000516	<--
NO---2001005746	A	20011126	2001NO-000005746	20011126	<--
NO------322120	B1	20060814			
MX---2001012172	A	20020722	2001MX-000012172	20011127	<--
ZA---2001010485	A	20030630	2001ZA-000010485	20011220	<--
IN----200101351	A	20050311	2001IN-000001351	20011221	<--
HK------1048444	A1	20051209	2003HK-000100617	20030123	<--
US-20050113386	A1	20050526	2004US-000994226	20041123	<--
US------7371756	B2	20080513			
NO---2006001562	A	20011126	2006NO-000001562	20060406	<--
NO------324230	B1	20070910			
US-20080119484	A1	20080522	2007US-000946149	20071128	<--
PRAI 1999EP-000109295	A	19990527	<--		
2000CA-002372668	A3	20000516	<--		
2000CN-000808135	A3	20000516	<--		
2000EP-000935031	A3	20000516	<--		
2004EP-000001441	A3	20000516	<--		

L48 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)

2000WO-EP0004376	W	20000516	<--	
2002US-000979922	A3	20020408	<--	
2004US-000994226	A3	20041123		

AB 1-[4-(5-Cyanoindol-3-yl)butyl]-4-(2-carbamoyl-benzofuran-5-yl)-piperazine (I) or a physiol. acceptable salt thereof is used for the manufacture of a medicament for the treatment of sub-type anxiety disorders chosen from the sub-types panic disorder with or without agoraphobia, obsessive-compulsive spectrum disorders, social phobia, post-traumatic stress disorder, acute stress indication or generalized-anxiety disorder, bipolar disorders, mania, dementia, substance-related disorders, sexual dysfunctions, eating disorders, obesity, anorexia and fibromyalgia. A preferred salt is I hydrochloride. For example, a mixture containing 1 kg I or a physiol. acceptable salt, 4 kg lactose, 1.2 kg potato starch, 0.2 kg talc, and 0.1 kg Mg stearate was tableted in the customary manner in such a way that each tablet comprises 10 mg of active ingredient.
IT **163521-08-2 163521-12-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. of cyanoindolylbutyl(carbamoylbenzofuranyl)-piperazine and its salts for treatment of anxiety and related disorders)
IT **163521-08-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. of cyanoindolylbutyl(carbamoylbenzofuranyl)-piperazine and its salts for treatment of anxiety and related disorders)
RN 163521-08-2 HCAPLUS
CN 2-Benzofurancarboxamide, 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-, hydrochloride (1:1) (CA INDEX NAME)

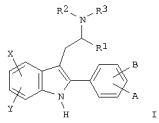


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

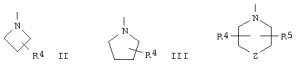
L48 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 1999:184232 HCAPLUS
DN 130:237469
TI Preparation of phenylindoles as 5-HT2A receptor ligands
IN Castro Pineiro, Jose Luis; Hutchins, Steven Michael; Lewis, Stephen John; Rowley, Michael; Smith, Adrian Leonard; Stevenson, Graeme Irvine
PA **Merck** Sharp & Dohme Limited, UK
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO-----9911619	A1	19990311	1998WO-GB0002616	19980901 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU-----9888766	A	19990322	1998AU-000088766	19980901 <--
US-----6486153	B1	20021126	2000US-000508046	20000303 <--
PRAI 1997GB-000018833	A	19970904	<--	
1998WO-GB0002616	W	19980901	<--	

OS MARPAT 130:237469
GI



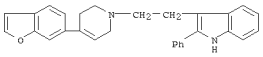
I



II III IV

AB The title compds. [I; A, B = H, halo, CN, etc.; X, Y = H, halo, alkyl, etc.; R1 = H, alkyl; R2 = H, Me, Et, etc.; R3 = alkyl, alkenyl, cycloalkyl, etc.; NR2R3 = II-IV, etc.; R4 = H, alkyl, alkoxyalkyl, etc.; R5 = H, alkyl, alkoxyalkyl; Z = O, S, NR6, CR7R8; R6 = H, alkyl, alkenyl, etc.; R7 = H, alkyl, heterocyclyl, etc.; R8 = H, Ph, AcO], selective antagonists of the human 5-HT2A receptor and therefore useful as pharmaceutical agents, especially in the treatment and/or prevention of adverse neurol. conditions, including psychotic disorders such as schizophrenia, were prepared E.g., a multi-step synthesis of I [A, B, X, Y = H; R1 = H; NR2R3 = piperidino], was given. Prepared compds. I were all found to possess a Ki of ≤ 100 nM for displacement of[3H]-ketanserin from the human 5-HT2A receptor, when expressed in Chinese hamster ovary (CHO) clonal cell lines.
IT **221282-03-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

L48 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)
(prepn. of phenylindoles as 5-HT2A receptor ligands)
IT **221282-03-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylindoles as 5-HT2A receptor ligands)
RN 221282-03-7 HCAPLUS
CN 1H-Indole, 3-[2-[4-(6-benzofuranyl)-3,6-dihydro-1(2H)-pyridinyl]ethyl]-2-phenyl- (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 1997:177658 HCAPLUS
DN 126:272161
OREF 126:52581a,52584a
TI EMD 68843, a serotonin reuptake inhibitor with selective presynaptic 5-HT1A receptor agonistic properties
AU **Bartoszyk, Gerd D.**; Hegenbart, Rainer; Ziegler, Herbert
CS Department of CNS-Research, CNS-Pharmacology, **Merck** KGaA, Darmstadt, D-64271, Germany
SO European Journal of Pharmacology (**1997**), 322(2/3), 147-153
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier
DT Journal
LA English
AB The 5-HT1A receptor agonist 8-hydroxy-(di-n-propylamino)tetralin (8-OH-DPAT; 0.55 mg/kg s.c.) and the 5-HT (5-hydroxytryptamine, serotonin) reuptake inhibitor/5-HT1A receptor ligand 5-[4-[4-(5-cyano-3-indolyl)-butyl]-1-piperazinyl]-benzofuran-2-carboxamide (EMD 68843; 55 mg/kg p.o.) inhibited ultrasonic vocalization in rats, an effect which was antagonized by the 5-HT1A receptor antagonist N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-ethyl]-N-(2-pyridyl)-cyclohexancarboxamide (WAY 100635; 1.0 mg/kg s.c.). 8-OH-DPAT decreased body temperature in rats, an effect which was also antagonized by WAY 100635, whereas EMD 68843 neither affected body temperature by itself nor interacted with 8-OH-DPAT or WAY 100635. The selective 5-HT reuptake inhibitor fluoxetine (100 mg/kg p.o.) had no effect on ultrasonic vocalization or body temperature Therefore EMD 68843 is suggested to be a 5-HT1A receptor agonist selective for presynaptic 5-HT1A receptors.
IT **188919-57-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(EMD 68843 behavioral effects as 5-HT1A receptor agonist)
IT **188919-57-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(EMD 68843 behavioral effects as 5-HT1A receptor agonist)
RN 188919-57-5 HCAPLUS
CN 2-Benzofurancarboxaldehyde, 5-[4-[4-(5-ethynyl-1H-indol-3-yl)butyl]-1-piperazinyl]- (CA INDEX NAME)

L48 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN
AN 1995:586488 HCAPLUS
DN 123:9463
OREF 123:1991a
TI Preparation of (indolylalkyl)piperidines and -piperazines as drugs.
IN Boettcher, Henning; **Seyfried, Christoph**; **Bartoszyk, Gerd**; Greiner, Hartmut
PA **Merck** Patent G.m.b.H., Germany
SO Ger. Offen., 12 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE-----4333254	A1	19950406	1993DE-004333254	19930930 <--
EP------648767	A1	19950419	1994EP-000114798	19940920 <--
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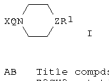

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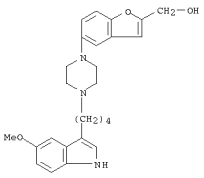
AB Title compds. [I; X = (HO-, alkoxy-, cyano-, halo-, R2CO-, R2CH2-substituted) 3-indolyl; R1 = (cyano-, HOCH2-, alkoxymethyl-, R2CO-substituted) benzofuran-5-yl, 2,3-dihydrobenzofuran-5-yl, chroman-6-yl, chroman-4-on-5-yl, 3-chromen-6-yl, chromen-4-on-6-yl; Q = (CH2)m; Z = N, CR3; R2 = OH, alkoxy, amino; R3 = H, OH, alkoxy; m = 2-4], were prepared having 5-HT1A agonist activity, etc. (no data). Thus, 3-(4-chlorobutyl)-5-methoxyindole and 1-(2-hydroxymethylbenzofuran-5-yl)piperazine were refluxed in MeCN to give 1-[4-(5-methoxyindol-3-yl)butyl]-4-(2-hydroxymethylbenzofuran-5-yl)piperazine.
IT **163521-02-6P 163521-03-7P 163521-06-0P**
163521-07-1P 163521-08-2P 163521-09-3P
163521-11-7P 163521-12-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (indolylalkyl)piperidines and -piperazines as drugs)
IT **163521-18-4 163521-19-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (indolylalkyl)piperidines and -piperazines as drugs)
IT **163521-02-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

L48 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2009 ACS on STN (Continued)
(prepn. of (indolylalkyl)piperidines and -piperazines as drugs)
RN 163521-02-6 HCAPLUS
CN 2-Benzofuranmethanol, 5-[4-[4-(5-methoxy-1H-indol-3-yl)butyl]-1-piperazinyl]- (CA INDEX NAME)



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L15          102 E3-6
                 E BOTTCHER HENNING/AU
L16            9 E3
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L17           51 E3-4
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L18           17 E3-5
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L19            2 E4-5
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L21          123 E4-8
                 E LEIBROCK J/AU
L22           43 E3-5
                 E SEYFRIED C/AU
L23          231 E3-6,E12-14
L24        36253 MERCK/CS,PA
L25           11 L11 AND L13-23
L26           11 L11 AND L24
L27            7 L25 AND L26
L28            4 L25 NOT L27
L29           16 L12 AND L13-24
L30           12 L12 AND L13-23
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L32            4 L29 NOT L31
L33           13 L12 NOT L31
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